or one of its multiples; hours, minutes, and seconds must be a thorn in the flesh of avid rationalisers; while even the SI units contain some compromises with what has been called purity.

So threatened, we ask only that the authorities decline in future to consider any proposal for changes in notation which come to them from any individual or group, however distinguished, unless the institutions which represent the clinicians of the nation shall have had a part in its making.

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A H JAMES
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SIR,—The controversy over SI units conducted through your correspondence columns and those of the *Lancet* has provided light entertainment for many. Curiosity decided me to page through a few issues of the two journals of the early fifties, the time at which the metric system and the milliequivalent were introduced into clinical medicine. Your leading article of 7 February 1953,[1] mentioning the advantages of the metric system, was followed over the weeks by a series of strangely familiar letters. Correspondents refer to the safety and convenience of the older system (imperial and avoirdupois) and the "difficulties in making a complete change."[2] The dangers of "misplacing decimal points" are mentioned and there are semiserious attempts at ridicule —a dose of 1 drachm per stone body weight is converted to "3·55 ml per 6·35 kg."[3] Small wonder that a French colleague found that "most of the objections expressed by your correspondents are so very childish."[4] Let us hope he has been spared the 1975 contributions.

Changes in reporting of electrolytes produced remarks on "the liberty with which certain blood components are expressed in milliequivalents."[5] The writer, fearing that "this makes for confusion and opens the door to serious dispensing errors," concluded that "for practical purposes it is surely more useful to retain mg per 100 ml—the form in which, I believe, most clinicians think, and of which they know the normal blood-levels."

Perhaps the most thought-provoking quotation is from your leading article.[1] "To follow this lead should not be too difficult for the medical profession even if, for a year or two, it entails a certain amount of extra thought. The lasting benefit would so outweigh the transient puzzling that medical men 20 years hence would look back in amazement at the reluctance of their seniors to institute the change."

I wonder, sir, would we dare to point a finger?

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[1] *British Medical Journal*, 1953, **1**, 320.
[2] Leak, W N, *British Medical Journal*, 1953, **1**, 619.
[3] Hewer, C L, *British Medical Journal*, 1953, **1**, 450.
[4] Mouchot, G, *British Medical Journal*, 1953, **1**, 1109.
[5] Ennis, J E, *Lancet*, 1953, **2**, 990.

Chemotherapy for breast cancer

SIR,—Your interesting leading article "Curability of breast cancer" (21 February, p 414) refers to trials in America. Perhaps it would not be out of place to remind your readers that the pioneer work in chemotherapy for breast cancer was begun in Bradford in 1957 by Dr (now Professor) R L Turner and the late Mr G Whyte Watson, and their first paper was published in the *BMJ* in 1959.[1] It is not generally appreciated how much is owed to these two pioneers.

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[1] Watson, G W, and Turner, R L, *British Medical Journal*, 1959, **1**, 1315.

Radiology and endoscopy in acute upper gastrointestinal bleeding

SIR,—I am interested in the paper by Dr G M Fraser and others (31 January, p 270) and the reaction to this by Dr K F R Schiller and his colleagues (14 February, p 393).

As a radiologist I have stated my opinion elsewhere that "endoscopy undertaken by an experienced endoscopist takes pride of place in the investigation of the acute upper tract bleed."[1] However, it is important to realise that emergency endoscopic services are not available to all and to take note of the remarks on this subject expressed by Forrest *et al.*[2] At the same time we should also remember that the patient suffering an acute bleed is admitted to the nearest acute hospital, whether emergency endoscopy is or is not available within 12-24 hours of the time of admission. Obviously radiology, as an alternative to endoscopy, has a part to play in this emergency service and, like endoscopy, must be undertaken early if we are to expect a high diagnostic yield.

The criticism by endoscopists that radiology may show a lesion but cannot demonstrate that this lesion is the source of bleeding is no longer valid. Double-contrast studies are capable of showing specific features characteristic of a bleeding point which are never reproduced in any other situation.[3] This additional information greatly enhances the value of emergency radiology.

It is interesting that Dr Schiller and his colleagues should refer to "this most recent attack on endoscopy, written by radiologists in defence of radiology." I recall numerous papers written by endoscopists in favour of endoscopy and questioning the role of radiology in the investigation of the acute bleed. Constructive co-operation and not empire-sustaining sharpshooting from either side would serve the best interest of the patient and give most help to the clinician responsible for the management of the case. Surely there is a happy medium based on an understanding of the needs and merits of the individual case and the facilities available at the time of admission. I agree with Mr F P McGinn and his colleagues (14 February, p 394) that "the two methods of investigation are complementary, but if a choice must lie between them then endoscopy should take precedence."

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[1] Scott-Harden, W G, in *Topics of Gastroenterology, 3*, ed S C Truelove and M J Goodman. Oxford, Blackwell Scientific, 1975.
[2] Forrest, J A H, Finlayson, N D C, and Shearman, D J C, *Lancet*, 1974, **2**, 394.
[3] Scott-Harden, W G, *Journal of the Royal College of Physicians of London*, 1974, **8**, 365.

Immunisation against whooping cough

SIR,—In writing to you to defend the papers by Dr Christine L Miller and Mr W B Fletcher (17 January, p 117) and by Dr N D Noah (p 128) Dr T M Pollock (14 February, p 396) dons a capacious mantle. He says that essential data were withheld from Dr Noah's paper "for the sake of brevity"—a matter which I should have thought concerned you, Sir, and Dr Noah. And he rebukes me for adhering to a basic tenet of epidemiology when I suggested that an association, however significant, between an independent variable (immunisation) and a dependent variable (disease) cannot be regarded as causal unless allowance is made for other variables known to influence susceptibility to the disease. Since the epidemiological data from Colindale discount all other variables, conclusions drawn from them are at best inferential. However, even without analysis of variables other than immunisation it is clear from both papers that the protection associated with immunisation is highly incomplete since 36% of all patients and 44% of patients aged 1-2 years described by Dr Miller and Mr Fletcher were fully immunised, as were 38% of the entire series presented by Dr Noah.

Dr N W Preston (14 February, p 396) seems to be in conflict with all of us. He despises notifications, so he presumably distrusts the Colindale data. But he agrees with their conclusions because he regards the new vaccine used by the Colindale workers as being effective because, in previous letters, he has said so. He considers that the decline in whooping cough is due to this new vaccine but does not say how he would explain the greater decline which occurred before it began to be used in 1968. He asks us to accept the new vaccine as being non-toxic because he says so and calls upon the world at large to provide evidence to the contrary. He asks me to provide evidence before criticising the Colindale data but does not hesitate to refute my evidence before it is published. He will find, incidentally, that I accept the desirability of bacteriological confirmation (who wouldn't?), but he must surely know that in practice whooping cough is a disease in which an experienced doctor or parent is as likely to reach a correct diagnosis as a bacteriologist.

Mrs Rosemary Fox (21 February, p 458) draws attention to the need to investigate the possibility that the new vaccine may occasionally be neurotoxic. In my view she is correct in requesting a retrospective investigation, for it may be some years before the prospective survey authorised by the DHSS yields useful evidence.

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Primary gout affecting the sternoclavicular joint

SIR,—The short report by Dr G R Sant and Mr E Dias (31 January, p 262) cannot be allowed to go unchallenged. The authors have committed two common errors in the diagnosis and management of this disease.

It is of course unjustifiable to diagnose gout of the sternoclavicular joint in an 18-year-old girl purely on the basis of raised plasma uric acid levels obtained at a time

when the patient was ill and taking drugs. These drugs may have included (for example) aspirin, which can be a potent cause of hyperuricaemia. Such a diagnosis would be acceptable only if urate crystals had been identified in the joint aspirate, a simple test which for some reason was neglected here. The information provided suggests that the patient actually had a pyogenic arthritis partly suppressed by antibiotics.

The second error was in management. Treating acute gout with a short course of allopurinol is not only useless but may actually be harmful by provoking a new attack.

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Serum creatine phosphokinase and malignant hyperpyrexia

SIR,—Professor M A Denborough's criticisms (15 November, p 408) of our findings (30 August, p 511) that serum CPK estimation is of little or no value in screening for malignant hyperpyrexia are invalid.

He states that 30% of muscle fibres taken from 54 normal individuals developed contracture with halothane. In a much larger series in our own laboratory we have found only one apparently normal muscle specimen which developed contracture with halothane. The reason for Professor Denborough's finding may be related to his choice of the rectus abdominis muscle for his study of normal controls. We consistently use the vastus medialis muscle and all our samples are taken across the motor point.

If false-positives were as numerous as he suggests this would be seen as a positive bias in our overall results (see table). Since the halothane-induced muscle contracture test was introduced in 1971[1] we have investigated 106 patients, of whom 48 (45%) developed halothane contracture. Even allowing for a number of patients being referred for this investigation who were found to have unrelated anaesthetic problems (for example, muscle spasm with suxamethonium without hyperpyrexia) this represents a positive result in 48 of 89 patients—that is, 54%. Thus our results are close to the 50% which could be anticipated for a condition inherited as a Mendelian dominant.

Muscle biopsy results for malignant hyperpyrexia

	1971	1972	1973	1974	1975 (up to 22.11)
Patients investigated ..	2	17	24	24	38
MHS+	2	7	13	11	15
MHS−	—	8	10	10	11
Unrelated conditions ..	—	2	3	3	9

MHS+ indicates halothane-induced contracture
MHS− indicates no halothane-induced contracture.

The slight positive bias in our results can be easily explained because among the 89 patients from malignant hyperpyrexia families 12 were "indexed" patients (that is, patients who had recovered from a clinically diagnosed episode of malignant hyperpyrexia). Even if Professor Denborough completely rejects the relevance of the halothane-induced muscle contracture as a satisfactory test for malignant hyperpyrexia susceptibility he surely cannot claim that serum CPK activity is of any value if 6 out of 12 indexed patients have consistently normal values (less than 60 U/l). It must be remembered that CPK estimations can often give falsely high values if the conditions for, and method of, venesection are not ideal. Blood should be taken without venous occlusion and the patient should not have exercised excessively for 48 hours before.

The more detailed in vitro tests quoted by Professor Denborough do not seem to be of any greater value or specificity than halothane-induced contracture. In our experience, if the latter is positive so are all the others.

Of much greater importance than the multiplicity of pharmacological tests used by Professor Denborough is the direct demonstration of myopathy by routine neurohistological techniques. All our patients have extensive histological and histochemical investigations and the excellent agreement between halothane-induced contracture and histological myopathy was shown in our paper. It is only in the light of these findings and their correlation that it is possible to demonstrate the inadequacy of serum CPK estimation as a screening test for malignant hyperpyrexia.

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E MARGARET MODGILL
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[1] Ellis, F R, *et al*, *British Journal of Anaesthesia*, 1971, **43**, 721.

Phenformin and lactic acidosis

SIR,—In lactic acidosis associated with phenformin at therapeutic dosage Professor P H Wise and others (10 January, p 70) give good evidence for a combined aetiology, involving both phenformin itself and co-existent disease (which may act via reduced removal of the drug). How much the diabetes contributes, however, will necessarily remain in doubt until a therapeutic use of phenformin is found in unrelated diseases. The main evidence at hand for the production of lactic acidosis by phenformin in non-diabetics comes from a very few cases of self-poisoning, in most of which the patient did not both survive and demonstrate a normal glucose tolerance. In this context the following case may be of some interest, supporting the view that toxic levels of phenformin are the crucial factor.

A healthy 28-year-old woman was admitted having ingested 3 g of phenformin and six capsules of pentobarbitone. On admission she was comatose with a normal respiratory rate (14/min). After 5½ hours she developed hyperpnoea which continued at 35-60/min for three days (but which resembled the hyperpnoea of salicylate poisoning rather than acidotic respiration and did not correlate with arterial pH). Arterial pH estimations varied from 7·20 to 7·38 over the first 60 hours despite administration of 23 200 mmol of $NaHCO_3$. Blood lactate at 39 hours was 30·6 mmol/l (276 mg/100 ml). Blood glucose at 5½ hours was 6·2 mmol/l (111 mg/100 ml), but fell to 1·2 mmol/l (22 mg/100 ml) at 20 hours despite 75 g of intravenous glucose. A further 75 g of intravenous glucose was needed to maintain normal levels over the next four hours. Mild ketonuria persisted for 36 hours. ECG showed very peaked T waves after 24 hours despite normal serum potassium. Consciousness was regained after 48 hours. Blood pressure and temperature were normal throughout. There were no clinical or laboratory signs of cardiovascular or renal disease, and glucose tolerance was normal some weeks later. The patient made a full recovery.

These clinical and biochemical features are similar to those seen in previously reported cases of phenformin-induced lactic acidosis with the exception of rather profound hypoglycaemia, which clearly may relate to the non-diabetic state, and the time scale of the drug intoxication.

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Beta-blockers in the treatment of chronic simple glaucoma

SIR,—I was interested to read your excellent concise leading article on this subject (24 January, p 180). For the information of some of your readers, however, I would like to suggest that there is some recent good evidence that an important contribution to reduction in intraocular pressure in humans is made by β-adrenergic blockade alone, whether or not a membrane-stabilising or initial β-mimetic effect may also be involved; Tenormin (atenolol), which is a pure β-adrenergic blocker, has been found to reduce intraocular pressure when given by mouth[1 2] and it has quantitatively a very similar effect to that of propranolol.[2 3] Another supportive observation is that DL-propranolol (which has both membrane-stabilising and β-blocking properties) was more effective in reducing intraocular pressure than D-propranolol (which has an equal membrane-stabilising but a much weaker β-blocking effect); the difference was more clearcut in glaucoma patients than in rabbits.[4]

Also, two longer-term studies do suggest that the effect is not short-lived[5 6]

These drugs reduce intraocular pressure in chronic closed-angle glaucoma but of course early operation is very much the treatment of choice in almost all cases of angle-closure glaucoma and most cases of chronic closed-angle glaucoma.

The place of β-adrenergic blockers in the treatment of the glaucomas is still undecided, especially if systemic administration is required, as your article indicated. However, as you also mentioned, the efficacy of pindolol eye drops[7] is encouraging because it has the significant advantage of not producing topical anaesthesia, unlike guttae propranolol, which are also effective.[9] Unfortunately guttae practolol,[9] as potent as guttae propranolol,[8] and without the local anaesthetic effect, may well carry the risk of the oculo-muco-cutaneous reaction even if not given systemically. We are awaiting the opportunity to test the effect of guttae Tenormin (atenolol).

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[1] Elliot, M J, Cullen, M, and Phillips, C I, *British Journal of Ophthalmology*, 1975, **59**, 296.
[2] Wettrell, K, and Pandolfi, M, *Experimental Eye Research*, 1975, **21**, 451.
[3] Macdonald, M J, Cullen, P M, and Phillips, C I, unpublished observations.
[4] Vale, J, and Phillips, C I, *Experimental Eye Research*, 1970, **9**, 902.
[5] Coté, G, and Drance, S M, *Canadian Journal of Ophthalmology*, 1968, **3**, 207.
[6] Pandolfi, M, and Öhrström, A, *Acta Ophthalmologica* 1974, **52**, 464.
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[8] Vale, J, Gibbs, A C C, and Phillips, C I, *British Journal of Ophthalmology*, 1972, **56**, 770.
[9] Vale, J, and Phillips, C I, *British Journal of Ophthalmology*, 1973, **57**, 210.